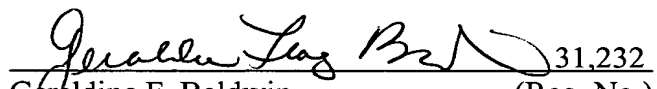
amendments, and the amendments are fully supported by the Specification of the subject application and the claims as originally filed. Accordingly, Applicants respectfully request that these amendments and remarks be entered and made of record in the present application..

CONCLUSION

Applicants respectfully request entry of the foregoing amendments to the specification and remarks in the file of the above-identified application. No fee is believed to be due for the submission of this Amendment. Should any fees be required, however, please charge such fees to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Respectfully submitted,

Dated: August 6, 2001



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(212) 790-9090
Attorneys For Applicants

Attachment:

Exhibit A: Marked up version of the replacement paragraphs of the specification

EXHIBIT A

Marked up Version of the Replacement Paragraphs of the Specification

Matter that has been deleted from the paragraphs is indicated by brackets and matter that has been added to the paragraphs is indicated by double underlining.

On page 1, at line 10, please amend the paragraph beginning "Priority is claimed" as follows:

This is a national stage application of International Application PCT/US99/19068, filed August 18, 1999, which was published under PCT Article 21(2) as PCT Publication No. WO 00/10602 in English. Priority is claimed to United States provisional applications Serial Nos. 60/096,997 and 60/096,996, both filed on August 18, 1998, both of which are incorporated by reference herein in their entireties. --

On page 9, at line 20, please amend the paragraph beginning, "Figures 6A-D" as follows:

Figures 6A-D. Targeting of the *lats* locus by homologous recombination. (A) Sequence alignment of human *lats* (h-*lats*) (SEQ ID NO: 2) and mouse *lats* (m-*lats*, partial sequence) (SEQ ID NO: 9). Arrow indicates the point at which the mouse *lats* gene was disrupted. (B) Targeting vector for positive-negative selection of homologous recombinants at the lats locus, with restriction map and the structure of the targeted lats locus. The vector is represented by the second line from the top, while the wild-type and mutant (i.e., disrupted) lats alleles are indicated by the top and bottom lines, respectively. The BamHI sites are indicated by "B", the EcoRI sites are indicated by "R", and the EcoRV sites are indicated by "RV". Exons are represented by filled rectangles. A BamHI/EcoRV double digest generates a 3.5 kb fragment from the wild-type allele and a 5.8 kb fragment from the disrupted allele, both of which are recognized by the probe shown, which is not contained in the targeting vector. In the vector and the mutant allele, the PGK-TK gene cassette and the PGK-neo fragment are denoted by open boxes labeled accordingly. (C) Southern blot of genomic DNA isolated from individual embryonic stem cell clones. The genotypes of the clones are indicated above the lanes with the "+/+" indicating wild-type clones, "+/-" indicating clones

heterozygous for the mutant allele, and "-/-" indicating clones homozygous for the mutant allele. (D) Western blot using anti-h-lats polyclonal antibody on lysates from 13.5 dpc (days post coitus) mouse embryonic fibroblasts indicating the absence of lats protein in the knock-out mice. The genotype of the clones is indicated above the lanes as in panel C.